Science 240:1759-1764 (1988); O'Shea, E. K. *et al.*, *Science* 243:538-542 (1989); McKnight, S. L., *Scientific American* 54-64, April 1991; Schmidt-Dorr. T. *et al.*, *Biochemistry* 30:9657-9664 (1991); Blondel, A. and Bedouelle, H. *Protein Engineering* 4:457-461 (1991), and the references cited in these papers.--

REMARKS

Applicants respectfully request entry of the Preliminary Amendment provided herewith for the purpose of correcting typographical errors in the originally filed specification and for the purpose of providing current patent and published application numbers wherever they are known. The justification for correction of the typographical errors is self-evident. None of the amendments constitute new matter.

Attached hereto at the **APPENDIX** is a marked-up version of the changes made to the specification by the current amendment. The attached page is captioned "**Version with markings to show changes made.**" Deleted text is shown with strike-through and new text is shown underlined.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: December 23, 2002

By: _____

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APPENDIX

Version with markings to show changes made

IN THE SPECIFICATION:

The paragraph spanning page 8, line 30 through page 9, line 7 has been amended as follows:

--Tolerance therapies incorporating either parenterally and orally administered diabetes autoantigens (including insulin and GAD) have been tried in experimental models and human subjects. However, the majority of human trials have met with disappointment. Furthermore, widespread application of peptide therapy in humans to treat autoimmune diabetes has been prevented by the observation that in some cases, peptide administration may actually accelerate disease progression (Pozzilli *et al.*, *Diabetologia* 43:1000-1004 [2000]; Gale, *Lancet* 356(9229):526-527 [2000]; Chaillous *et al.*, *Lancet* 356:545-549 [2000]; Blanas *et al.*, *Science* 274:1707-1709 [1996]; McFarland, *Science* 274(5295):2037 [1996]; and Bellmann *et al.*, *Diabetologia* 41:844-847 ~~844-887~~ [1998]).--

The paragraph on page 18, spanning lines 16 through 30 has been amended as follows:

--The terms "receptor comprising an immune receptor tyrosine-based inhibitory motif (ITIM)" and "ITIM-containing receptor" are used to refer to a receptor containing one or more immune receptor tyrosine-based inhibitory motifs, ITIMs. The ITIM motif can be generally represented by the formula Val/Ile-Xaa-PTyr-Xaa-Xaa-Leu/Val (where Xaa represents any amino acid). ITIM-containing receptors include, without limitation, FcγRIIb, gp49b1/gp91 (Arm *et al., J. Biol. Chem.* 266:15966-73 (1991)), p91/PIR-B (Hayami *et al., J. Biol. Chem.* 272:7320-7 (1997)), LIR1-3, 5, 8, LAIR-1; CD22 (van Rossenberg *et al., J. Biol. Chem.*, 276(16):12967-12973 (2001) ~~January 4, 2001~~); CTL-4, CD5, p58/70/140 KIR, PIRB2-5; NKB1, Ly49 A/C/E/F/G, NKG2-A/B, APC-R, CD66, CD72, PD-1, SHPS-1, SIRP-α1, IL T1-5, MIR7, 10, hMIR(HM18), hMIR(HM9), Fas(CD95), TGFβ-R, TNF-R1, IFN-γ-R (α- and β-chains), mast cell function Ag, H2-M, HLA-DM, CD1, CD1-d, CD46, c-cbl, Pyk2/FADK2, P130 Ca rel prot, PGDF-R, LIF, LIR-R, CIS, SOCS13 and 3, as reviewed in Sinclair NR *et al., supra*. Ligands for many of these receptors are also known, such as, e.g. the ligand for CD95 is called CD95 ligand,

the ligands for CTLA-4 are CD80 and CD86, the ligands of IFN-γ receptor is IFN-γ, etc. Ligands for CD22 comprise the basic binding motif Nau5Ac-a(2,6)-Lac, and are discussed, for example in van Rossenberg *et al.,* 2001, *supra.*--

The paragraph spanning page 59, line 24 through page 60, line 2 has been amended as follows:

--In a further specific embodiment, the two polypeptide sequences (including variants of the native sequences) are dimerized by amphiphilic helices. It is known that recurring copies of the amino acid leucine (Leu) in gene regulatory proteins can serve as teeth that "zip" two protein molecules together to provide a dimer. For further details about leucine zippers, which can serve as linkers for the purpose of the present invention, see for example: Landschulz, W. H., *et al. Science* 240:1759-1764 (1988); O'Shea, E. K. *et al.*, *Science* ~~243; 38-542~~ 243:538-542 (1989); McKnight, S. L., *Scientific American* 54-64, April 1991; Schmidt-Dorr. T. *et al.*, *Biochemistry* 30:9657-9664 (1991); Blondel, A. and Bedouelle, H. *Protein Engineering* 4:457-461 (1991), and the references cited in these papers.--